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(54) Title: RECEPTOR FINGERPRINTING, SENSORY PERCEPTION, AND BIOSENSORS OF CHEMICAL SENSANTS

(57) Abstract: The use of sensory G protein-coupled receptors that recognize chemical sensants, particularly those involving olfactory and taste receptors; polypeptide fragments and mutants thereof; classes of such receptors; polynucleotides encoding such receptors, fragments and mutants thereof, and representatives of receptor classes; genetic vectors including such polynucleotides; and cells and non-human organisms engineered to express such receptor complexes, fragments and mutants of an olfactory or taste receptor, and representatives of receptor classes to simulate sensory perception of odorants and tastants is described. The use of such products as a biosensor or a components thereof to detect, identify, measure, or otherwise process the event of binding between the receptor and its cognate ligand (*i.e.*, chemical sensant) is also described. The invention has application, for example, in the design and formulation of odorant and tastant compositions.

WO 01/98526 A2



Claims:

1. A method for representing sensory perception of one or more odorants comprising:
 - 5 (a) providing a representative class of n olfactory receptors or ligand-binding domains thereof;
 - (b) measuring values X_1 to X_n representative of at least one activity of the one or more odorants selected from the group consisting of binding of the one or more odorants to the ligand-binding domain of at least one of the n olfactory receptors, activating at least one of the n olfactory receptors with the one or more odorants, and blocking at least one of the n olfactory receptors with the one or more odorants; and
 - 10 (c) generating a representation of sensory perception from the values X_1 to X_n ;
- 15 wherein at least one of the n olfactory receptors has an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 57, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 67, SEQ ID NO: 69, SEQ ID NO: 71, SEQ ID NO: 73, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 79, SEQ ID NO: 81, SEQ ID NO: 83, SEQ ID NO: 85, SEQ ID NO: 87, SEQ ID NO: 89, SEQ ID NO: 91, SEQ ID NO: 93, SEQ ID NO: 95, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 105, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 115, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 121, SEQ ID NO: 123, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 133, SEQ ID NO: 135, SEQ ID NO: 137, SEQ ID NO: 139, SEQ ID NO: 141, SEQ ID NO: 143, SEQ ID NO: 145, SEQ ID NO: 147, SEQ ID NO: 149, SEQ ID NO: 151, SEQ ID NO: 153, SEQ ID NO: 155, SEQ ID NO: 157, SEQ ID NO: 159, SEQ ID NO: 161, SEQ ID NO: 163, SEQ ID NO: 165, SEQ ID NO: 167, SEQ ID NO: 169,
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511.

2. The method of Claim 1, wherein at least one of the olfactory receptors
specifically recognizes the odorant, and there are between 5 and 350 of the n olfactory
10 receptors selected from the listed amino acid sequences.

3. The method of Claim 1, wherein at least two different activities are measured
to provide the values X_1 to X_n .

15 4. The method of Claim 1, wherein each odorant receptor is expressed in cells,
and the cells expressing each odorant receptor are located at an identifiable position.

5. The method of Claim 1, wherein at least one olfactory receptor is soluble, and
binding of odorant to a ligand-binding domain of the soluble olfactory receptor is
20 measured in solution.

6. The method of Claim 1, wherein at least one olfactory receptor is in solid state,
and binding of odorant to a ligand-binding domain of the solid-state olfactory receptor
is measured on a substrate.

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7. The method of Claim 1, wherein the value measured for binding is above a
preset limit for specific binding to olfactory receptors.

8. The method of Claim 1, wherein the value measured for activating an olfactory
30 receptor is derived from a signal selected from the group consisting of intracellular
 Ca^{2+} , cAMP, cGMP and IP3.

9. The method of Claim 1, wherein the value measured for activating an olfactory receptor is above a preset limit for specific activation.
10. The method of Claim 1, wherein the value measured for blocking an olfactory
5 receptor is at least a reduction in binding of the odorant or activation by the odorant.
11. The method of Claim 1, wherein the representation of sensory perception is generated with a neural network.
- 10 12. A biosensor comprised of the n ligand-binding domains or olfactory receptors of Claim 1.
13. A method for producing a database of odorant representations comprising:
(a) providing one or more known odorants and
15 (b) generating a representation of the one or more known odorants in accordance with the method of Claim 1 to produce the database.
14. A database produced by Claim 13.
- 20 15. A method of identifying an unknown odorant comprising:
(a) measuring values X_1 to X_n representative of at least one activity selected from the group consisting of binding the unknown odorant to a ligand-binding domain of at least one of n olfactory receptors, activating at least one of n olfactory receptors with the unknown odorant, and blocking at
25 least one of n olfactory receptors with the unknown odorant;
(b) generating a representation of the unknown odorant from the values X_1 to X_n ; and
(c) comparing the unknown odorant's representation to the database of Claim 14 to identify the known odorant which is most similar in
30 representation.
16. A method of producing an artificial odorant comprising:

- 5 (a) measuring values X_1 to X_n representative of at least one activity selected from the group consisting of binding a desirable odorant to a ligand-binding domain of at least one of n olfactory receptors, activating at least one of n olfactory receptors with a desirable odorant, and blocking at least one of n olfactory receptors with a desirable odorant;
- (b) generating a representation of the desirable odorant from the values X_1 to X_n ;
- 10 (c) decomposing the desirable odorant's representation into representations of known odorants from the database of Claim 14 or superposing known odorants' representations from the database to reproduce the desirable odorant; and
- (d) formulating the known odorants to reproduce sensory perception of the desirable odorant and thereby produce the artificial odorant.

15 17. An artificial odorant produced by Claim 16.

18. A method of identifying a primary odorant related to sensory perception comprising:

- 20 (a) providing a representative class of n olfactory receptors or ligand-binding domains thereof,
- (b) measuring at least one activity of a odorant selected from the group consisting of binding of the candidate odorant to the ligand-binding domain of at least one of the n olfactory receptors and activating with the candidate odorant at least one of the n olfactory receptors, and
- 25 (c) identifying the candidate odorant as a primary odorant if only one or less than 10% of the representative class of n olfactory receptors is bound or activated;

wherein at least one of the n olfactory receptors has an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID

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 511.

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19. A primary odorant identified by Claim 18.

20. A method of identifying a compound which blocks activation by a odorant of
 at least one olfactory receptor comprising:

- 25 (a) producing a structurally-related candidate compound from a ligand of
 the at least one olfactory receptor,
 (b) measuring activation by the odorant of the at least one olfactory
 receptor with the candidate compound, and
 (c) identifying the candidate compound as a compound which blocks
 30 activation if activation of the at least one olfactory receptor is reduced or
 inhibited;

wherein at least one of the olfactory receptors has an amino acid sequence selected
 from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID

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25 21. The method of Claim 20, wherein the ligand is a primary odorant.

22. A compound which blocks activation of an olfactory receptor identified by
Claim 20.

AOLFR52 sequences:

MLGPAYNHTMETPASFLI.VGIPGLQSSHI.WI.AISI.SAMYITALLGNTLIVTAIWMDSTRHEPMY
 CFLCVLAAVDIVMASSVVPKMVSIFCSGDSISFSACFTQMFFVHLATAVETGLLLTMAFDYRV
 AICKPLHYKRILTPQVMLGMSMAVITRAVTFMTPLSWMMNHLPCGNSNVVVHSYCKHIALAR
 5 LACADPVPSSLYSLIGSSLMVGSVDVAFIAASYILILRAVFDLSSKTAQLKALSTCGSHVGVMAly
 YLPGMASIYAAWLGQDIVPLHTQVLLADLYVIIPATLNPDIYGMRTKQLLEGIWSYLMHFLFDH
 SNLGS (SEQ ID NO: 99)

ATGCTGGGTCCAGCTTACAACCACACAATGGAAACCCCTGCCTCCTTCCTCCTTGTGGGTA
 10 TCCCAGGACTGCAATCTTCACATCTTTGGCTGGCTATCTCACTGAGTGCCATGTACATCAC
 AGCCCTGTTAGGAAACACCCTCATCGTGAAGTCAATCTGGATGGATTCCACTCGGCATGAG
 CCCATGTATTGCTTTCTGTGTGTTCTGGCTGCTGTGGACATTGTTATGGCCTCCTCCGTGGT
 ACCCAAGATGGTGAGCATCTTCTGCTCGGGAGACAGCTCCATCAGCTTTAGTGCTTGTTC
 ACTCAGATGTITTTTGTCCACTTAGCCACAGCTGTGGAGACGGGGCTGCTGCTGACCATGG
 15 CTTTTGACCGCTATGTAGCCATCTGCAAGCCTCTACACTACAAGAGAATTCTCAGCCTCA
 AGTGATGCTGGGAATGAGTATGGCCGTCACCATCAGAGCTGTACATTTCATGACTCCACTG
 AGTTGGATGATGAATCATCTACCTTTCTGTGGCTCCAATGTGGTTGTCCACTCCTACTGTAA
 GCACATAGCTTTGGCCAGGTTAGCATGTGCTGACCCCGTGCCAGCAGTCTCTACAGTCTG
 ATGGTTCTCTCTTATGTTGGGCTCTGATGTGGCCTTCATTGCTGCCTCCTATATCTTAAT
 20 TCTCAGGGCAGTATTTGATCTCTCCTCAAAGACTGCTCAGTTGAAAGCATTAAAGCACATGT
 GGCTCCCATGTGGGGGTTATGGCTTTGTACTATCTACCTGGGATGGCATCCATCTATGCGG
 CCTGGTTGGGGCAGGATATAGTGCCCTTGACACCCCAAGTGCTGCTAGCTGACCTGTACGT
 GATCATCCAGCCACITTAATCCCATCATCTATGGCATGAGGACCAACAATTGCTGGAG
 GGAATATGGAGTTATCTGATGCACTTCTCTTTGACCACTCCAACCTGGGTTTCATGA (SEQ
 25 ID NO: 100)

AOLFR54 sequences:

MSDSNLSNHLDPDFFLTGIPGLEAAHFVIAIPFCAMYLVALVGNAALILVIAMDNALHAPMY
 LFLCLSLTDLALSSTVTPKMLAILWLHAGEISFGGCLAQMFCVHSIYALESSILLAMAFDRYVA
 30 ICNPLRYTTILNHAIVIGRIGFVGLFRSVAIVSPFIFLLRRLPYCGHRVMTHTYCEHMGARLACA
 NITVNIVYGLTVALLAMGLDSILIAISYGFIHVAVHLP SHDAQHKALSTCGSHIGILVFYIPAFF
 SFLTHRFHHEVPHVHIFLANLYVLVPPVLPILYGARTKEIRSRLKLLHLGKTSI (SEQ ID
 NO: 101)

ATGTCAGATTCCAACCTCAGTGATAACCATCTTCCAGACACCTTCTTCTTAACAGGGATCC
 CAGGGCTGGAGGCTGCCCACCTTCTGGATTGCCATCCCTTTCTGTGCCATGTATCTTGTAGC
 ACTGGTTGGAAATGCTGCCCTCATCCTGGTCAATGCCATGGACAATGCTCTTCATGCACCT
 ATGTACCTCTTCCCTCTGCCTTCTCTCACTCACAGACCTGGCTCTCAGTTCTACCACTGTGCC
 CAAGATGCTGGCCATTTTGTGGCTCCATGCTGGTGAGATTTCCTTTGGTGGATGCCCTGGCC
 40 CAGATGTTTTGTGTCCATTCTATCTATGCTCTGGAGTCCCTCGATTCTACTTGCCATGGCCTT
 TGATAGGTATGTGGCTATCTGTAAACCATTAAGGTATACAACCATTTCAACCATGCTGTC
 ATAGGCAGAATTGGCTTTGTGGGCTATTCCGTAAGTGTGGCTATTGTCTCCCCCTTCATCTT
 CTTGCTGAGGCGACTCCCCTACTGTGGTCAACCGTGTGATGACACACATACTGTGAGCAT
 ATGGGCATCGCCGACTGGCCTGTGCCAACATCACTGTCAATATTGTCTATGGGCTAACTG
 45 TGGCTCTGCTGGCCATGGGACTGGATTCCATTCTCATTGCCATTTCTATGGCTTTATCCTC
 CATGCAGTCTTTACCTTCCATCTCATGATGCCAGCACAAAGCTCTGAGTACCTGTGGCT
 CCCACATTGGCATCATCCTGGTTTTCTACATCCCTGCCTTCTTCTCCTTCCACCCACCGC
 TTTGGTCAACACGAAGTCCCCAAGCATGTGCACATCTTCTGGCTAATCTCTATGTGCTGG
 TGCCCTCTGTACTCAATCCTATTCTCTATGGAGCTAGAACCAAGGAGATTGCGAGTCGACT
 50 TCTAAAACCTGCTTACCTGGGGAAGACTTCAATATGA (SEQ ID NO: 102)

AOLFR57 sequences:

MSFQVTYMFYLHWTMEKSNNSTLFILLGFSQNKNEIVLCFVLFVFCYIAIWMGNLLIMISITCTQ
 LIHQPMYFFLNLYSLSDLCYTSTVTPKLMVDLLAERKTISYNNCMQLFTTHFFGGIEIFLTGM
 55 AYDRYVAICKPLHYTIIMSQRKCNTHIVCCTGGFIHSASQFLLTIFVFPFCGPNEIDHYFCDVYPL
 KLACSNHIMIGLLVIANSGLIALVTFVLLSYVFIYITIRAYSAERRSKALATCSSHVIVVVLFF

